```
=> d his

     (FILE 'REGISTRY' ENTERED AT 12:08:38 ON 25 APR 2005)
                DEL HIS Y
                ACT ROOKE2/A
               ---------
L1              STR
L2              SCR 963
L3              SCR 2006 OR 1950
L4   (      3830)SEA FILE=REGISTRY SSS FUL L1 AND L2 NOT L3
L5   (      1371)SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND 1/NC
L6   (      1100)SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT (S OR N OR F OR CL OR
L7          1097 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND NO RSD/FA
               ---------
                E A-LACTALBUMIN/CN
L8            1 S E3
L9          121 S ALPHA LACTALBUMIN

     FILE 'HCAPLUS' ENTERED AT 12:17:34 ON 25 APR 2005
L10           68 S L8 OR L9
L11        92506 S L7
L12         4953 S LACTALBUMIN
L13         4957 S L12 OR L10
L14           56 S L11 AND L13
L15         3641 S L12 (L) ALPHA
L16         3646 S L10 OR L15
L17           33 S L16 AND L11
L18            3 S L16 (L) COFACTOR?
L19           34 S L18 OR L17
                SET SFIELD BI
L20          281 S K79 OR D82 OR D84 OR D87 OR D88
L21            0 S L20 AND L16
L22            0 S L20 AND L11
L23            0 S L12 AND L20
L24            0 S S70R OR S70 R
L25            0 S S 70R OR S 70 R
L26           25 S FATTY ACID# (L) L12
L27           20 S FATTY ACID# (L) L16
L28           12 S L27 NOT L19
L29       276946 S MUTATION?
L30            0 S L29 AND L28
L31            1 S CALCIUM AND L28
L32           35 S L31 OR L19
L33           16 S L16 AND COFACTOR
L34           10 S L33 AND (L11 OR FATTY ACID#)
L35            4 S L34 NOT L19
L36           38 S L35 OR L19
L37           14 S L36 AND (63 OR 1)/SC,SX
L38            5 S L36 AND DELIVER?
L39           14 S L38 OR L37
L40           24 S L36 NOT L39
```

```
=> fil reg
FILE 'REGISTRY' ENTERED AT 12:28:49 ON 25 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   24 APR 2005  HIGHEST RN 849094-71-9
DICTIONARY FILE UPDATES:  24 APR 2005  HIGHEST RN 849094-71-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que stat l7
L1              STR

HO2C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~C~~Me
   1    2   3   4   5   6   7   8   9  10  11  12  13  14  15  16  17  18


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  18

STEREO ATTRIBUTES: NONE
L2              SCR 963
L3              SCR 2006 OR 1950
L4   (      3830)SEA FILE=REGISTRY SSS FUL L1 AND L2 NOT L3
L5   (      1371)SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND 1/NC
L6   (      1100)SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT (S OR N OR F OR CL OR
                 BR OR I OR SI OR P)/ELS
L7          1097 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND NO RSD/FA
```

```
=> d que nl9
'NL9' IS NOT VALID HERE

=> d que l9
L9            121 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALPHA LACTALBUMIN


=> d l9

L9   ANSWER 1 OF 121  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   721871-39-2  REGISTRY
ED   Entered STN:  03 Aug 2004
CN   α-Lactalbumin (Bubalus bubalis isoform A) (9CI)   (CA INDEX
     NAME)
FS   PROTEIN SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
                1 REFERENCES IN FILE CA (1907 TO DATE)
                1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d que l8;d l8
L8            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  A-LACTALBUMIN/CN


L8   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   9051-29-0  REGISTRY *
* Use of this CAS Registry Number alone as a search term in other STN files may
  result in incomplete search results.  For additional information, enter HELP
  RN* at an online arrow prompt (=>).
ED   Entered STN:  16 Nov 1984
CN   Lactalbumins, α-  (CA INDEX NAME)
OTHER NAMES:
CN   α-Lactalbumin
CN   α-Lactalbumins
CN   Alpha-lactalbumins
CN   Calcium complexes α-lactalbumins
CN   Lactalbumins, α-, calcium complexes
CN   Lactalbumins, alpha-
CN   Lactose synthetase B protein
MF   Unspecified
CI   MAN, CTS
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS,
       CBNB, CHEMCATS, CIN, CSCHEM, EMBASE, IPA, MSDS-OHS, NIOSHTIC, PHAR,
       TOXCENTER

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
                2 REFERENCES IN FILE CA (1907 TO DATE)
                2 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> d que l9
L9          121 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALPHA LACTALBUMIN
```

```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:29:19 ON 25 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 25 Apr 2005  VOL 142 ISS 18
FILE LAST UPDATED: 24 Apr 2005  (20050424/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que nos l39
L1              STR
L2              SCR 963
L3              SCR 2006 OR 1950
L4   (      3830)SEA FILE=REGISTRY SSS FUL L1 AND L2 NOT L3
L5   (      1371)SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND 1/NC
L6   (      1100)SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT (S OR N OR F OR CL OR
                 BR OR I OR SI OR P)/ELS
L7          1097 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND NO RSD/FA
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  A-LACTALBUMIN/CN
L9           121 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALPHA LACTALBUMIN
L10           68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR L9
L11        92506 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L12         4953 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTALBUMIN/OBI
L15         3641 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 (L) ALPHA/OBI
L16         3646 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 OR L15
L17           33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L11
L18            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 (L) COFACTOR?/OBI
L19           34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 OR L17
L33           16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND COFACTOR
L34           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND (L11 OR FATTY ACID#)
L35            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 NOT L19
L36           38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 OR L19
L37           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND (63 OR 1)/SC,SX
L38            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND DELIVER?
L39           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L37


=> d que nos l40
L1              STR
L2              SCR 963
L3              SCR 2006 OR 1950
L4   (      3830)SEA FILE=REGISTRY SSS FUL L1 AND L2 NOT L3
```

```
L5  (      1371) SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 AND 1/NC
L6  (      1100) SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT (S OR N OR F OR CL OR
                 BR OR I OR SI OR P)/ELS
L7         1097 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 AND NO RSD/FA
L8            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  A-LACTALBUMIN/CN
L9          121 SEA FILE=REGISTRY ABB=ON  PLU=ON  ALPHA LACTALBUMIN
L10          68 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR L9
L11       92506 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L12        4953 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTALBUMIN/OBI
L15        3641 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 (L) ALPHA/OBI
L16        3646 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 OR L15
L17          33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L11
L18           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 (L) COFACTOR?/OBI
L19          34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 OR L17
L33          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND COFACTOR
L34          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND (L11 OR FATTY ACID#)
L35           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 NOT L19
L36          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L35 OR L19
L37          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND (63 OR 1)/SC,SX
L38           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND DELIVER?
L39          14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 OR L37
L40          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 NOT L39


=> d .ca hitstr l39 1-14;d ibib ab l40 1-24
THE ESTIMATED COST FOR THIS REQUEST IS 73.64 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L39  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2004:515417  HCAPLUS
DOCUMENT NUMBER:         141:116685
TITLE:                   Treatment of skin papillomas with topical .
                         alpha.-lactalbumin-oleic acid
AUTHOR(S):               Gustafsson, Lotta; Leijonhufvud, Irene; Aronsson,
                         Annika; Mossberg, Ann-Kristin; Svanborg, Catharina
CORPORATE SOURCE:        Department of Microbiology, Immunology, and
                         Glycobiology, Institute of Laboratory Medicine,
                         University of Lund, Lund, Swed.
SOURCE:                  New England Journal of Medicine (2004), 350(26),
                         2663-2672
                         CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER:               Massachusetts Medical Society
DOCUMENT TYPE:           Journal
LANGUAGE:                English
ED   Entered STN:  27 Jun 2004
AB   We studied the effect on skin papillomas of topical application of a
     complex of a-lactalbumin and oleic acid (often referred to as human
     α-lactalbumin made lethal to tumor cells [HAMLET]) to establish
     proof of the principle that α-lactalbumin-oleic acid kills
     transformed cells but not healthy, differentiated cells.  Forty patients
     with cutaneous papillomas that were resistant to conventional treatment
     were enrolled in a randomized, placebo-controlled, double-blind study, in
     which α-lactalbumin-oleic acid or saline placebo was applied daily
     for three weeks and the change in the volume of each lesion was recorded.
     After this first phase of the study, 34 patients participated in the
     second phase, an open-label trial of a three-week course of
     α-lactalbumin-oleic acid.  Approx. two years after the end of the
     open-label phase of the study, 38 of the original 40 patients were examined,
     and long-term follow-up data were obtained.  In the first phase of the
     study, the lesion volume was reduced by 75 percent or more in all 20
```

patients in the α-lactalbumin-oleic acid group, and in 88 of 92 papillomas; in the placebo group, a similar effect was evident in only 3-of 20 patients (15 of 74 papillomas) (P<0.001). After the patients in the initial placebo group had been treated with α-lactalbumin-oleic acid in the second phase of the study, a median reduction of 82 percent in lesion volume was observed At follow-up two years after the end of the second phase, all lesions had completely resolved in 83 percent of the patients treated with α-lactalbumin-oleic acid, and the time to resolution was shorter in the group originally assigned to receive α-lactalbumin-oleic acid than among patients originally in the placebo group (2.4 vs. 9.9 mo; P<0.01). No adverse reactions were reported, and there was no difference in the outcomes of treatment between immunocompetent and immunosuppressed patients. Treatment with topical α-lactalbumin-oleic acid has a beneficial and lasting effect on skin papillomas.

CC **1-6** (Pharmacology)

IT Papilloma
(cutaneous; α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

IT Skin, neoplasm
(papilloma; α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

IT Drug **delivery** systems
(topical, solution; α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

IT **Lactalbumins**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -, solution containing oleic acid; α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

IT Antitumor agents
Human
(α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

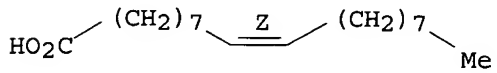
IT **112-80-1D**, Oleic acid, solution containing α -**lactalbumin**, biological studies
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

IT **112-80-1D**, Oleic acid, solution containing α -**lactalbumin**, biological studies
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -**lactalbumin**-oleic acid topical solution in treatment of skin papillomas)

RN 112-80-1 HCAPLUS

CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN

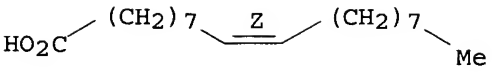
ACCESSION NUMBER: 2004:467679 HCAPLUS
DOCUMENT NUMBER: 141:22609
TITLE: Nutritional compositions for galactosamine hepatopathy suppression and macrophage immunosuppression.
INVENTOR(S): Kume, Hisae; Yamaguchi, Makoto; Mizumoto, Kenji; Sasaki, Hajime
PATENT ASSIGNEE(S): Meiji Dairies Corporation, Japan
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047566	A1	20040610	WO 2003-JP14918	20031121

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-339948 A 20021122
ED Entered STN: 10 Jun 2004
AB The present inventors discovered that the onset of galactosamine hepatopathy is suppressed by nutritional compns. comprising as essential ingredients: whey protein hydrolyzates, lecithin and oils and fats high in oleic acid which are able to improve the lipid metabolism, and palatinose having an insulin-sparing effect. Furthermore, the whey protein hydrolyzate included in the nutritional compns. was found to suppress endotoxin-induced TNF-a and interleukin 6 (IL-6) production in macrophages.
IC ICM A23L001-305
ICS A23L001-09; A23L001-29; A23L001-30; A61P001-16; A61P029-00; A61K031-7016; A61K035-20
CC 17-6 (Food and Feed Chemistry)
Section cross-reference(s): **63**
IT **Lactalbumins**
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(α -; nutritional compns. for galactosamine hepatopathy suppression and macrophage immunosuppression)
IT **112-80-1**, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fats and oils high in; nutritional compns. for galactosamine hepatopathy suppression and macrophage immunosuppression)
IT **112-80-1**, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fats and oils high in; nutritional compns. for galactosamine hepatopathy suppression and macrophage immunosuppression)
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:325339 HCAPLUS
DOCUMENT NUMBER: 141:49306
TITLE: No Need To Be HAMLET or BAMLET To Interact with Histones: Binding of Monomeric α - **Lactalbumin** to Histones and Basic Poly-Amino Acids
AUTHOR(S): Permyakov, Serge E.; Pershikova, Irina V.; Khokhlova, Tatyana I.; Uversky, Vladimir N.; Permyakov, Eugene A.
CORPORATE SOURCE: Institute for Biological Instrumentation, Russian Academy of Sciences, Moscow, 142290, Russia
SOURCE: Biochemistry (2004), 43(19), 5575-5582
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Apr 2004
AB The ability of a specific complex of human α-lactalbumin with oleic acid (HAMLET) to induce cell death with selectivity for tumor and undifferentiated cells was shown recently to be mediated by interaction of HAMLET with histone proteins irreversibly disrupting chromatin structure (Duringer, C., et al. ,2003). Here we show that monomeric α-lactalbumin (α-LA) in the absence of fatty acids is also able to bind efficiently to the primary target of HAMLET, histone HIII, regardless of Ca2+ content. Thus, the modification of α-LA by oleic acid is not required for binding to histones. We suggest that interaction of neg. charged α-LA with the basic histone stabilizes apo-α-LA and destabilizes the Ca2+-bound protein due to compensation for excess neg. charge of α-LA's Ca2+-binding loop by pos. charged residues of the histone. Spectrofluorimetric curves of titration of α-LA by histone H3 were well approximated by a scheme of cooperative binding of four α-LA mols. per mol. of histone, with an equilibrium dissociation constant of 1.0 μM. Such a stoichiometry of binding implies that the binding process is not site-specific with respect to histone and likely is driven by just electrostatic interactions. Co-incubation of pos. charged poly-amino acids (poly-Lys and poly-Arg) with α-LA resulted in effects which were similar to those caused by histone HIII, confirming the electrostatic nature of the α-LA-histone interaction. In all cases that were studied, the binding was accompanied by aggregation. The data indicate that α-lactalbumin can be used as a basis for the design of antitumor agents, acting through disorganization of chromatin structure due to interaction between α-LA and histone proteins.
CC 6-3 (General Biochemistry)
Section cross-reference(s): **1**
ST histone H3 **alpha lactalbumin** electrostatic binding polyamino acid; HAMLET BAMLET histone H3 **alpha lactalbumin**
IT Histones
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(H3; binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT Self-association
(aggregation; binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT Antitumor agents
Dissociation constant
Drug design
Molecular association
Stoichiometry
(binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT Denaturation
(protein, thermal; binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT **Lactalbumins**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(α -; binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT Electrostatic force
(α -LA-histone interaction; binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT **112-80-1D**, Oleic acid, complexes with human or bovine α -**lactalbumin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to)

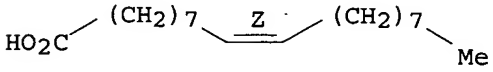
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT 24937-47-1, Poly-Arginine 25104-18-1, Poly-Lysine 25212-18-4, Poly-Arginine 38000-06-5, Poly-Lysine
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to design of antitumor agents)

IT **112-80-1D**, Oleic acid, complexes with human or bovine α -**lactalbumin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of monomeric α -**lactalbumin** to histones and basic poly-amino acids in relation to)

RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:214382 HCAPLUS
DOCUMENT NUMBER: 140:332008
TITLE: Human α -**Lactalbumin** Made Lethal to Tumor Cells (HAMLET) Kills Human Glioblastoma Cells in Brain Xenografts by an Apoptosis-Like Mechanism and Prolongs Survival
AUTHOR(S): Fischer, Walter; Gustafsson, Lotta; Mossberg, Ann-Kristin; Gronli, Janne; Mork, Sverre; Bjerkvig, Rolf; Svanborg, Catharina
CORPORATE SOURCE: Immunology and Glycobiology, Department of Microbiology, Institute of Laboratory Medicine, University of Lund, Swed.
SOURCE: Cancer Research (2004), 64(6), 2105-2112
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 18 Mar 2004
AB Malignant brain tumors present a major therapeutic challenge because no selective or efficient treatment is available. Here, we demonstrate that intratumoral administration of human α-lactalbumin made lethal to tumor cells (HAMLET) prolongs survival in a human glioblastoma (GBM) xenograft model, by selective induction of tumor cell apoptosis. HAMLET is a protein-lipid complex that is formed from α-lactalbumin when the protein changes its tertiary conformation and binds oleic acid as a cofactor. HAMLET induces apoptosis in a wide range of tumor cells in vitro, but the therapeutic effect in vivo has not been examined In this study, invasively growing human GBM tumors were established in nude rats (Han:rnu/rnu Rowett, n = 20) by transplantation of human GBM biopsy spheroids. After 7 days, HAMLET was administered by intracerebral convection-enhanced **delivery** for 24 h into the tumor area; and α-lactalbumin, the native, folded variant of the same protein, was used as a control. HAMLET reduced the intracranial tumor volume and delayed the onset of pressure symptoms in the tumor-bearing rats. After 8 wk, all α-lactalbumin-treated rats had developed pressure symptoms, but the HAMLET-treated rats remained asymptomatic. Magnetic resonance imaging scans revealed large differences in tumor volume (456 vs. 63 mm3). HAMLET caused apoptosis in vivo in the tumor but not in adjacent intact brain tissue or in nontransformed human astrocytes, and no toxic side effects were observed The results identify HAMLET as a new candidate in cancer therapy and suggest that HAMLET should be addnl. explored as a novel approach to controlling GBM progression.
CC **1-6** (Pharmacology)
Section cross-reference(s): 14
ST **alpha lactalbumin** HAMLET glioblastoma apoptosis antitumor
IT Neuroglia, neoplasm
(glioblastoma; human α -**lactalbumin** made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival)
IT Antitumor agents
Apoptosis
Brain, neoplasm
Disease models
Human

Molecular modeling
(human α -**lactalbumin** made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival)

IT Tertiary structure
(protein; human α -**lactalbumin** made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival)

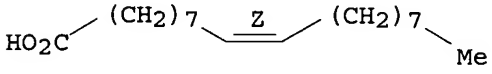
IT **Lactalbumins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -; human α -**lactalbumin** made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival)

IT **112-80-1**, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complexes with human α -**Lactalbumin** (HAMLET); human α -**lactalbumin** made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival)

IT **112-80-1**, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complexes with human α -**Lactalbumin** (HAMLET); human α -**lactalbumin** made lethal to tumor cells (HAMLET) kills human glioblastoma cells in brain xenografts by an apoptosis-like mechanism and prolongs survival)

RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:927818 HCAPLUS
DOCUMENT NUMBER: 140:141302
TITLE: Lipids as **cofactors** in protein folding: Stereo-specific lipid-protein interactions are required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells)
AUTHOR(S): Svensson, Malin; Mossberg, Ann-kristin; Pettersson, Jenny; Linse, Sara; Svanborg, Catharina
CORPORATE SOURCE: Department of Microbiology, Immunology and Glycobiology (MIG), Institute of Laboratory Medicine, Lund University, Lund, Swed.
SOURCE: Protein Science (2003), 12(12), 2805-2814
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Nov 2003
AB Proteins can adjust their structure and function in response to shifting environments. Functional diversity is created not only by the sequence but by changes in tertiary structure. Here, the authors present evidence

that lipid cofactors may enable otherwise unstable protein folding variants to maintain their conformation and to form novel, biol. active complexes. The authors have identified unsatd. C18 fatty acids in the cis conformation as the cofactors that bind apo-α-lactalbumin (apo-α-LA) and form HAMLET (human α-LA made lethal to tumor cells), a complex of human α-LA and oleic acid (C18:1:9 cis). The complexes were formed on an ion-exchange column, were stable in a molten globule-like conformation, and had attained the novel biol. activity. The protein-fatty acid interaction was specific, as saturated C18 fatty acids, or unsatd. C18:1 trans conformers were unable to form complexes with apo-α-LA, as were fatty acids with shorter or longer C chains. Unsatd. cis fatty acids other than C18:1:9 cis were able to form stable complexes, but these were not active in the apoptosis assay. The results demonstrate that stereospecific lipid-protein interactions can stabilize partially unfolded conformations and form mol. complexes with novel biol. activity. The results offer a new mechanism for the functional diversity of proteins, by exploiting lipids as essential, tissue-specific cofactors in this process.

CC 6-3 (General Biochemistry)
Section cross-reference(s): **1**

ST protein folding lipid **cofactor**; HAMLET formation antitumor activity apoptosis lipid protein interaction; **lactalbumin alpha** folding lipid **cofactor**

IT Antitumor agents
(HAMLET; lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT Apoptosis
Human
Protein folding
(lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT Stereochemistry
(stereospecificity; lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT Fatty acids, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unsatd., C18; lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT **Lactalbumins**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(α -, complexes with oleic acid (HAMLET); lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human

α -**lactalbumin** made lethal to tumor cells))

IT **Lactalbumins**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(α -; lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

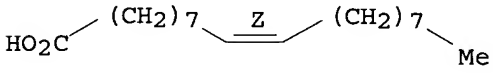
IT **112-80-1D**, Oleic acid, complexes with α -**lactalbumin** (HAMLET)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT **112-80-1**, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT **112-80-1D**, Oleic acid, complexes with α -**lactalbumin** (HAMLET)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

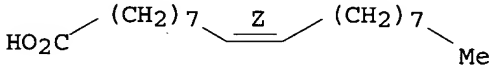
Double bond geometry as shown.



IT **112-80-1**, Oleic acid, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(lipids act as **cofactors** in protein folding as shown by stereospecific lipid-protein interactions required to form HAMLET (human α -**lactalbumin** made lethal to tumor cells))

RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:927817 HCAPLUS
DOCUMENT NUMBER: 140:107208
TITLE: α -**Lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for the conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells)
AUTHOR(S): Svensson, Malin; Fast, Jonas; Mossberg, Ann-kristin; Dueringer, Caroline; Gustafsson, Lotta; Hallgren, Oskar; Brooks, Charles L.; Berliner, Lawrence; Linse, Sara; Svanborg, Catharina
CORPORATE SOURCE: Department of Microbiology, Immunology and Glycobiology (MIG), Institute of Laboratory Medicine, Lund University, Lund, Swed.
SOURCE: Protein Science (2003), 12(12), 2794-2804
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Nov 2003
AB HAMLET (human α-lactalbumin made lethal to tumor cells) is a complex of human α-lactalbumin (I) and oleic acid (C18:1:9 cis) that kills tumor cells by an apoptosis-like mechanism. Previous studies have shown that a conformational change is required to form HAMLET from I, and that a partially unfolded conformation is maintained in the HAMLET complex. This study examined if unfolding of I was sufficient to induce cell death. The authors used bovine I Ca2+-binding site mutant D87A, which is unable to bind Ca2+, and thus remains partially unfolded regardless of solvent conditions. The D87A mutant protein was found to be inactive in the apoptosis assay, but could readily be converted to a HAMLET-like complex in the presence of oleic acid. BAMLET (bovine α-lactalbumin made lethal to tumor cells) and D87A-BAMLET complexes were both able to kill tumor cells. This activity was independent of the Ca2+ site, as HAMLET maintained a high affinity for Ca2+ but D87A-BAMLET was active with no Ca2+ bound. It was concluded that partial unfolding of I is necessary but not sufficient to trigger cell death, and that the activity of HAMLET is defined both by the protein and the lipid cofactor. Furthermore, a functional Ca2+-binding site is not required for conversion of I to the active complex or to cause cell death. This suggests that the lipid cofactor stabilizes the altered fold without interfering with the Ca2+ site.
CC 6-3 (General Biochemistry)
Section cross-reference(s): **1**
ST **lactalbumin alpha** unfolding apoptosis induction HAMLET formation antitumor activity; BAMLET formation antitumor activity **alpha lactalbumin** unfolding apoptosis induction
IT Protein folding
(unfolding; α -**lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells))
IT **Lactalbumins**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α -, complexes with oleic acid (HAMLET); α -**lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells))
IT **Lactalbumins**

RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); BIOL (Biological study); PROC (Process)
(α -; α -**lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT Antitumor agents
Apoptosis
Human
(α -**lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells))

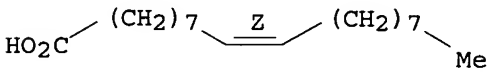
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(a functional Ca2+-binding site in α -**lactalbumin** is not required for its conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells) or to induce apoptosis)

IT **112-80-1D**, Oleic acid, complexes with human α -**lactalbumin** (HAMLET)
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α -**lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells))

IT **112-80-1D**, Oleic acid, complexes with human α -**lactalbumin** (HAMLET)
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(α -**lactalbumin** unfolding is not sufficient to cause apoptosis, but is required for conversion to HAMLET (human α -**lactalbumin** made lethal to tumor cells))

RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:913191 HCAPLUS
DOCUMENT NUMBER: 139:375001
TITLE: Active complex of α -**lactalbumin** (HAMLET) and **cofactor** for the treatment of papillomas
INVENTOR(S): Svanborg, Catherine
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095490	A1	20031120	WO 2003-IB2366	20030508
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1506233	A1	20050216	EP 2003-727868	20030508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRIORITY APPLN. INFO.:			GB 2002-10464 A	20020508
			WO 2003-IB2366 W	20030508

ED Entered STN: 21 Nov 2003

AB The invention discloses the use of a biol. active complex of α-lactalbumin, selected from HAMLET (human α-lactalbumin made lethal to tumor cells) or a biol. active modification thereof, or a biol. active fragment of either of these, in the preparation of a medicament for use in the treatment of papillomas, e.g. cutaneous papillomas.

IC ICM C07K014-76
ICS A23L001-305; A23J001-20; A23J003-08; A61K038-38; A61K047-12; A61K035-20

CC **1-6** (Pharmacology)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C18-unsatd., C18:1:9 and C18:1:11, **cofactor**; active complex of α -**lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C18-unsatd., C18:1; active complex of α -**lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)

IT Anion exchange chromatography
Antitumor agents
Gel permeation chromatography
Human
Ion exchange chromatography
Mutation
Papilloma
(active complex of α -**lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)

IT Caseins, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(active complex of α -**lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)

IT Bos taurus
(bovine α -**lactalbumin**; active complex of α -**lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)

IT Milk
(casein fraction; active complex of α - **lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)
IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**cofactor**; active complex of α - **lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)
IT **Lactalbumins**
RL: NPO (Natural product occurrence); PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(α -; active complex of α - **lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(and calcium binding site; active complex of α - **lactalbumin** (HAMLET) and **cofactor** for papilloma treatment)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:912976 HCAPLUS
DOCUMENT NUMBER: 139:386408
TITLE: Preparation of sustained-release formulations of protein drugs
INVENTOR(S): Lee, Hee-Yong; Kim, Jung-Soo; Lee, Ji-Suk; Kim, Jung-In; Seo, Yun-Mi; Lim, Chae-Jin; Kim, Sung-Kyu; Jung, Young-Hwan; Chang, Seung-Gu; Choi, Ho-Il
PATENT ASSIGNEE(S): Peptron Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094887	A1	20031120	WO 2003-KR921	20030509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2003087975	A	20031115	KR 2003-29407	20030509
PRIORITY APPLN. INFO.:			KR 2002-25522 A	20020509

ED Entered STN: 21 Nov 2003
AB The present invention relates to a sustained-release formulation comprising protein as an active ingredient, and a preparation method thereof. According to the present invention, the sustained-release formulation

contains protein drugs, e.g., human growth hormone, that are encapsulated in biodegradable hydrophobic matrixes, such as fatty acids, glycerides, and phospholipids, as pharmaceutically active forms by forming complexes with sulfated polysaccharides. The sustained-release formulation prepared by the present invention can be used to effectively treat a disease without frequent injections by keeping the protein concentration at a sufficiently high level for a long period when injected in vivo once. For example, human growth hormone (GH) and dextran sulfate (DS) were mixed with 1% aqueous acetic acid solution to final concns. of 3 mg/mL GH and 15 mg/mL
DS. The mixture was spray dried and microparticles (mean diameter 3.2 μm) were obtained. The GH-DC complex particles (500 mg) were spray coated with 50 mL of a methylene chloride solution containing 5 mg/mL tristearin to prepare tristearin-coated microparticles containing GH (mean diameter 6.5 μm).

IC ICM A61K009-00
CC **63-6** (Pharmaceuticals)
IT Drug **delivery** systems
(microparticles, sustained-release; encapsulation of protein drugs and sulfated polysaccharides in hydrophobic matrixes for sustained drug release)
IT Drug **delivery** systems
(sustained-release; encapsulation of protein drugs and sulfated polysaccharides in hydrophobic matrixes for sustained drug release)
IT **Lactalbumins**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -; encapsulation of protein drugs and sulfated polysaccharides in hydrophobic matrixes for sustained drug release)
IT 57-10-3, Palmitic acid, biological studies **57-11-4**, Stearic acid, biological studies 124-07-2, Caprylic acid, biological studies 130-85-8, Pamoic acid 544-63-8, Myristic acid, biological studies 555-43-1, Tristearin 1338-41-6, Span 60 4539-70-2, Distearoyl phosphatidylcholine 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 12441-09-7D, Sorbitan, fatty acid esters 19698-29-4, Dipalmitoyl phosphatidic acid 24967-94-0, Dermatan sulfate 26780-50-7, RG 502H 31566-31-1, Glyceryl monostearate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation of protein drugs and sulfated polysaccharides in hydrophobic matrixes for sustained drug release)
IT **57-11-4**, Stearic acid, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(encapsulation of protein drugs and sulfated polysaccharides in hydrophobic matrixes for sustained drug release)
RN 57-11-4 HCAPLUS
CN Octadecanoic acid (9CI) (CA INDEX NAME)

$HO_2C-(CH_2)_{16}-Me$

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:719503 HCAPLUS
DOCUMENT NUMBER: 139:224401
TITLE: Biologically active complex
INVENTOR(S): Svanborg, Catharina; Svensson, Malin Wilhelmina
PATENT ASSIGNEE(S): Swed.

SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074547	A2	20030912	WO 2003-IB1293	20030307
WO 2003074547	A3	20031127		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1485413	A2	20041215	EP 2003-710101	20030307
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005085416	A1	20050421	US 2003-506903	20030307
PRIORITY APPLN. INFO.:			GB 2002-5347 A	20020307
			WO 2003-IB1293 W	20030307

ED Entered STN: 14 Sep 2003

AB A biol. active complex comprising alpha-lactalbumin or a variant of alpha-lactalbumin which is in the apo folding state, or a fragment of either of any of these, and a cofactor which stabilizes the complex in a biol. active form, provided that any fragment of alpha-lactalbumin or a variant thereof comprises a region corresponding to the region of α-lactalbumin which forms the interface between the alpha and beta domains, and further provided that when the complex comprises native alpha-lactalbumin, the cofactor is other than C18:1:9 cis fatty acid. These complexes have therapeutic applications for example in the treatment of cancer and as antibacterial agents.

IC ICM C07K

CC **1-5** (Pharmacology)

ST **alpha lactalbumin cofactor** complex
anticancer antibacterial agent

IT Infection
(bacterial; biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT Antibacterial agents
Antitumor agents
Apoptosis
Conformation
Human
Molecular association
Neoplasm
(biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT Drug **delivery** systems
(carriers; biol. active complex of α -

lactalbumin and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT Mutation
(of α -**lactalbumin**; biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(unsatd., complexes with α -**lactalbumins**; biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT **Lactalbumins**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -, complexes; biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

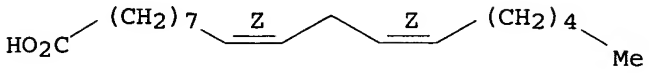
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT **60-33-3D**, Linoleic acid, complexes with α -**lactalbumins** **112-80-1D**, Oleic acid, complexes with α -**lactalbumins** 373-49-9D, Palmitoleic acid, complexes with α -**lactalbumins** **463-40-1D**, Linolenic acid, complexes with α -**lactalbumins** **506-17-2D**, complexes with α -**lactalbumins** **506-26-3D**, γ-Linolenic acid, complexes with α -**lactalbumins** 506-32-1D, Arachidonic acid, complexes with α -**lactalbumins** **593-39-5D**, Petroselinic acid, complexes with α -**lactalbumins** 5561-99-9D, complexes with α -**lactalbumins**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

IT **60-33-3D**, Linoleic acid, complexes with α -**lactalbumins** **112-80-1D**, Oleic acid, complexes with α -**lactalbumins** **463-40-1D**, Linolenic acid, complexes with α -**lactalbumins** **506-17-2D**, complexes with α -**lactalbumins** **506-26-3D**, γ-Linolenic acid, complexes with α -**lactalbumins** **593-39-5D**, Petroselinic acid, complexes with α -**lactalbumins**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. active complex of α -**lactalbumin** and **cofactor** such as cis-fatty acids as anticancer and antibacterial agents in relation to removal of calcium ions or calcium binding site)

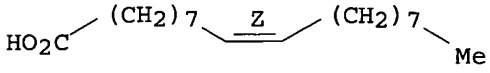
RN 60-33-3 HCAPLUS
CN 9,12-Octadecadienoic acid (9Z,12Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



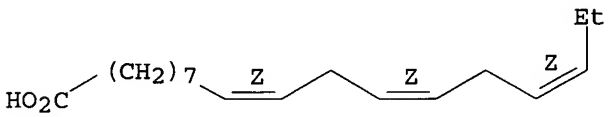
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



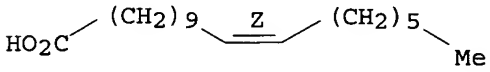
RN 463-40-1 HCAPLUS
CN 9,12,15-Octadecatrienoic acid, (9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



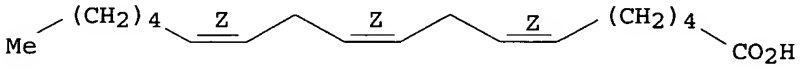
RN 506-17-2 HCAPLUS
CN 11-Octadecenoic acid, (11Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



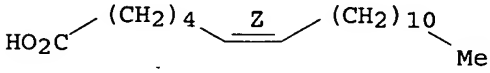
RN 506-26-3 HCAPLUS
CN 6,9,12-Octadecatrienoic acid, (6Z,9Z,12Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 593-39-5 HCAPLUS
CN 6-Octadecenoic acid, (6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L39 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:379409 HCAPLUS
DOCUMENT NUMBER: 139:332086
TITLE: HAMLET kills tumor cells by an apoptosis-like mechanism-cellular, molecular, and therapeutic aspects
AUTHOR(S): Svanborg, Catharina; Agerstam, Helena; Aronson, Annika; Bjerkvig, Rolf; Dueringer, Caroline; Fischer, Walter; Gustafsson, Lotta; Hallgren, Oskar; Leijonhuvud, Irene; Linse, Sara; Mossberg, Ann-Kristin; Nilsson, Hanna; Pettersson, Jenny; Svensson, Malin
CORPORATE SOURCE: Institute of Laboratory Medicine, Department of Microbiology, Immunology and Glycobiology, Lund University, Lund, 221 00, Swed.
SOURCE: Advances in Cancer Research (2003), 88, 1-29
CODEN: ACRSAJ; ISSN: 0065-230X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 19 May 2003
AB A review. HAMLET (human α-lactalbumin made lethal to tumor cells) is a protein-lipid complex that induces apoptosis-like death in tumor cells, but leaves fully differentiated cells unaffected. This review summarizes the information on the in vivo effects of HAMLET in patients and tumor models, on the tumor cell biol., and on the mol. characteristics of the complex. HAMLET limits the progression of human glioblastomas in a xenograft model and removes skin papillomas in patients. This broad anti-tumor activity includes >40 different lymphomas and carcinomas and apoptosis is independent of p53 or bcl-2. In tumor cells, HAMLET enters the cytoplasm, translocates to the perinuclear area, and enters the nuclei, where it accumulates. HAMLET binds strongly to histones and disrupts the chromatin organization. In the cytoplasm, HAMLET targets ribosomes and activates caspases. The formation of HAMLET relies on the propensity of α-lactalbumin to alter its conformation when the strongly bound Ca2+ ion is released and the protein adopts the apo-conformation that exposes a new **fatty acid** binding site. Oleic acid (C18:1,9 cis) fits this site with high specificity, and stabilizes the altered protein conformation. The results illustrate how protein folding variants may be beneficial, and how their formation in peripheral tissues may depend on the folding change and the availability of the lipid **cofactor.** One example is the acid pH in the stomach of the breast-fed child that promotes the formation of HAMLET. This mechanism may contribute to the protective effect of breastfeeding against childhood tumors. We propose that HAMLET should be explored as a novel approach to tumor therapy.
CC **1-0** (Pharmacology)
IT **Lactalbumins**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -, HAMLET; HAMLET kills tumor cells by an apoptosis-like mechanism and cellular and mol. and therapeutic aspects therein)
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:173458 HCAPLUS
DOCUMENT NUMBER: 138:215259

TITLE: Use of milk serum apoprotein in the prophylaxis or treatment of microbial or viral infection.
INVENTOR(S): Folan, Michael Anthony; Brady, Damien
PATENT ASSIGNEE(S): Westgate Biological Ltd., Ire.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018049	A2	20030306	WO 2002-IE121	20020820
WO 2003018049	A3	20031106		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1427436	A2	20040616	EP 2002-796345	20020820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005501863	T2	20050120	JP 2003-522566	20020820
US 2005042299	A1	20050224	US 2004-487616	20041018
PRIORITY APPLN. INFO.:			IE 2001-780 A	20010823
			WO 2002-IE121 W	20020820

ED Entered STN: 07 Mar 2003

AB The present invention relates to use of a milk apoprotein or a mixture thereof to prevent or treat microbial or viral infection of the human or animal body. It is believed that this is achieved by inhibiting adhesion of potential pathogens. More preferably, at least one milk apoprotein or a mixture thereof is administered, simultaneously or sequentially, with either or both of at least one free fatty acid or a mixture thereof or a monoglyceride thereof; and/or at least one organic acid or a salt or ester thereof or a mixture thereof. The active agent(s) may be **delivered** by means of a pharmaceutically acceptable **delivery** system which includes parenteral solns., ointments, eye drops, nasal sprays, intravaginal devices, surgical dressings, medical foods or drinks, oral health-care formulations and medicaments for mucosal applications.

IC A61K038-17; A61K035-30; A23L001-03; A61K007-16; A61K007-40; A61K038-117; A61K031-20; A61K038-17; A61K003-119

CC **1-5** (Pharmacology)
Section cross-reference(s): **63**

IT Cosmetics
(as **delivery** system; use of milk serum apoproteins in combination with fatty acids and organic acids in prophylaxis or treatment of microbial or viral infection)

IT Chewing gum
Dentifrices
Mouthwashes
(**delivery** system; use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)

IT Drug **delivery** systems
(nasal sprays; use of milk serum apoprotein in prophylaxis or treatment

of microbial or viral infection)
IT Drug **delivery** systems
(nasal; use of milk serum apoproteins in combination with fatty acids and organic acids in prophylaxis or treatment of microbial or viral infection)
IT Drug **delivery** systems
(ointments; use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)
IT Drug **delivery** systems
(ophthalmic; use of milk serum apoproteins in combination with fatty acids and organic acids in prophylaxis or treatment of microbial or viral infection)
IT Drug **delivery** systems
(oral; use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)
IT Drug **delivery** systems
(solns., ophthalmic; use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)
IT Drug **delivery** systems
(topical; use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)
IT Candida albicans
Drug **delivery** systems
Milk
Mouth, disease
(use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)
IT Drug **delivery** systems
(vaginal, vaginal creams or gels; use of milk serum apoprotein in prophylaxis or treatment of microbial or viral infection)
IT **Lactalbumins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α -, apolipoprotein derived from; use of milk serum apoproteins in combination with fatty acids and organic acids in prophylaxis or treatment of microbial or viral infection)
IT 50-21-5, Lactic acid, biological studies 50-21-5D, Lactic acid, salts or esters 57-10-3, Palmitic acid, biological studies **57-11-4**, Stearic acid, biological studies **60-33-3**, Linoleic acid, biological studies 68-04-2, Trisodium citrate 77-92-9, Citric acid, biological studies 77-92-9D, Citric acid, salts or esters 79-10-7, Propenoic acid, biological studies 79-10-7D, Propenoic acid, salts or esters 79-14-1, Glycolic acid, biological studies 79-14-1D, Glycolic acid, salts or esters 79-31-2, Isobutyric acid 80-69-3, Tartronic acid 80-69-3D, Tartronic acid, salts or esters 107-92-6, Butyric acid, biological studies 107-93-7, Trans-2-Butenoic acid 107-93-7D, Trans-2-Butenoic acid, salts or esters 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-16-7D, Maleic acid, salts or esters 110-17-8, Fumaric acid, biological studies 110-17-8D, Fumaric acid, salts or esters 110-94-1, Glutaric acid 110-94-1D, Glutaric acid, salts or esters **112-80-1**, Oleic acid, biological studies 124-04-9, Adipic acid, biological studies 124-07-2, Caprylic acid, biological studies 141-82-2, Malonic acid, biological studies 141-82-2D, Malonic acid, salts or esters 142-62-1, Caproic acid, biological studies 143-07-7, Lauric acid, biological studies 144-62-7, Oxalic acid, biological studies 144-62-7D, Oxalic acid, salts or esters 334-48-5, Capric acid 373-49-9, Palmitoleic acid **463-40-1**, α-Linolenic acid 473-81-4, Glyceric acid 473-81-4D, Glyceric acid, salts or esters 503-64-0, Cis-2-Butenoic acid 503-64-0D, Cis-2-Butenoic acid, salts or

esters **506-26-3**, Gamma linolenic acid 506-32-1, Arachidonic acid 526-83-0, Tartaric acid 526-83-0D, Tartaric acid, salts or esters 544-63-8, Myristic acid, biological studies 994-36-5, Sodium citrate 6915-15-7, Malic acid 6915-15-7D, Malic acid, salts or esters 7632-05-5, Sodium phosphate 25496-72-4, Oleic acid monoglyceride 26402-22-2, Capric acid monoglyceride 26402-23-3, Caproic acid monoglyceride 26402-26-6, Caprylic acid monoglyceride 26545-74-4, Linoleic acid monoglyceride 26545-75-5 26657-96-5, Palmitic acid monoglyceride 26699-71-8 26999-06-4, Butyric acid monoglyceride 27214-38-6, Myristic acid monoglyceride 27215-38-9, Lauric acid monoglyceride 31152-46-2, Tetracosenoic acid 31566-31-1, Stearic acid monoglyceride 32839-30-8, Eicosapentaenoic acid 55030-83-6 60130-63-4, Succinic acid monoglyceride 62207-91-4 124151-74-2, γ-Linolenic acid monoglyceride 139534-61-5 179092-15-0 500787-54-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of milk serum apoproteins in combination with fatty acids and organic acids in prophylaxis or treatment of microbial or viral infection)

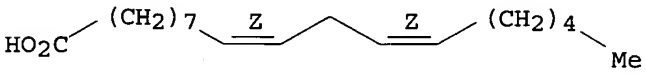
IT **57-11-4**, Stearic acid, biological studies **60-33-3**, Linoleic acid, biological studies **112-80-1**, Oleic acid, biological studies **463-40-1**, α-Linolenic acid **506-26-3**, Gamma linolenic acid
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of milk serum apoproteins in combination with fatty acids and organic acids in prophylaxis or treatment of microbial or viral infection)

RN 57-11-4 HCAPLUS
CN Octadecanoic acid (9CI) (CA INDEX NAME)

$HO_2C-(CH_2)_{16}-Me$

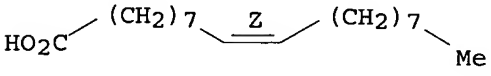
RN 60-33-3 HCAPLUS
CN 9,12-Octadecadienoic acid (9Z,12Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



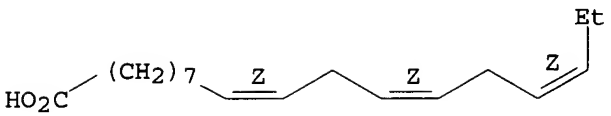
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



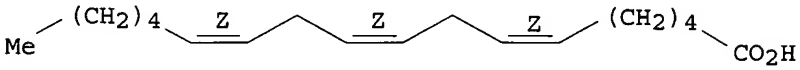
RN 463-40-1 HCAPLUS
CN 9,12,15-Octadecatrienoic acid, (9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 506-26-3 HCAPLUS
CN 6,9,12-Octadecatrienoic acid, (6Z,9Z,12Z)- (9CI) (CA INDEX NAME)

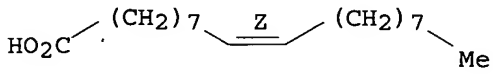
Double bond geometry as shown.



L39 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:710499 HCAPLUS
DOCUMENT NUMBER: 138:88796
TITLE: HAMLET- complex from human milk that induces apoptosis in tumor cells but spares healthy cells
AUTHOR(S): Svensson, Malin; Dueringer, Caroline; Hallgren, Oskar; Mossberg, Ann-Kristine; Hakansson, Anders; Linse, Sara; Svanborg, Catharina
CORPORATE SOURCE: Department of Microbiology, Immunology and Glycobiology (MIG), Institute of Laboratory Medicine, Lund University, Lund, S-223 62, Swed.
SOURCE: Advances in Experimental Medicine and Biology (2002), 503(Integrating Population Outcomes, Biological Mechanisms and Research Methods in the Study of Human Milk and Lactation), 125-132
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 19 Sep 2002
AB A review. The human α-lactalbumin made lethal to tumor cells (HAMLET) is a naturally occurring mol. complex in human milk that targets immature cells and tumor cells and that activates programmed cell death in those cells, sparing healthy cells. It consists of a-lactalbumin and the stabilizing cofactor oleic acid (C 18:1). Mols. such as HAMLET can a have a protective function in the breast fed child. HAMLET is one of several naturally occurring surveillance mols. that purge unwanted cells from the local tissues and drive the intestinal mucosa towards maturity. By inducing apoptosis, HAMLET may reduce the pool of potentially malignant cells that could serve as nuclei for future tumor development and explain the reduced frequency of cancer in breast-fed individuals.
CC 17-0 (Food and Feed Chemistry)
Section cross-reference(s): 1, 14
IT **Lactalbumins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α -; HAMLET complex from human milk induces apoptosis in tumor cells and reduces cancer in breast-fed individuals)
IT **112-80-1**, 9-Octadecenoic acid (9Z)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stabilizing cofactor of HAMLET complex; HAMLET complex from human milk induces apoptosis in tumor cells and reduces cancer in breast-fed individuals)

IT **112-80-1**, 9-Octadecenoic acid (9Z)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(stabilizing cofactor of HAMLET complex; HAMLET complex from human milk induces apoptosis in tumor cells and reduces cancer in breast-fed individuals)
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:270393 HCAPLUS
DOCUMENT NUMBER: 133:37880
TITLE: Conversion of α -**lactalbumin** to a protein inducing apoptosis
AUTHOR(S): Svensson, M.; Hakansson, A.; Mossberg, A.-K.; Linse, S.; Svanborg, C.
CORPORATE SOURCE: Department of Microbiology, Immunology and Glycobiology (MIG), Institute of Laboratory Medicine, Lund University, Lund, S-223 62, Swed.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(8), 4221-4226
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Apr 2000
AB In this study α-lactalbumin was converted from the regular, native state to a folding variant with altered biol. function. The folding variant was shown to induce apoptosis in tumor cells and immature cells, but healthy cells were resistant to this effect. Conversion to HAMLET (human α-lactalbumin made lethal to tumor cells) required partial unfolding of the protein and a specific **fatty acid**, C18:1, as a necessary **cofactor.** Conversion was achieved with α-lactalbumin derived from human milk whey and with recombinant protein expressed in Escherichia coli. We thus have identified the folding change and the **fatty acid** as two key elements that define HAMLET, the apoptosis-inducing functional state of α-lactalbumin. Although the environment in the mammary gland favors the native conformation of α-lactalbumin that serves as a specifier in the lactose synthase complex, the conditions under which HAMLET was formed resemble those in the stomach of the nursing child. Low pH is known to release Ca2+ from the high-affinity Ca2+-binding site and to activate lipases that hydrolyze free **fatty acids** from milk triglycerides. We propose that this single amino acid polypeptide chain may perform vastly different biol. functions depending on its folding state and the in vivo environment. It may be speculated that mols. like HAMLET can aid in lowering the incidence of cancer in breast-fed children by purging to tumor cells from the gut of the neonate.
CC **1-6** (Pharmacology)
ST lactalbumin protein apoptosis antitumor **fatty acid**
IT **Fatty acids**, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(C18:1; conversion of α -**lactalbumin** to a protein inducing apoptosis)

IT Antitumor agents
Apoptosis
(conversion of α -**lactalbumin** to a protein inducing apoptosis)

IT **Lactalbumins**
RL: BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(α -; conversion of α -**lactalbumin** to a protein inducing apoptosis)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L39 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:355804 HCAPLUS
DOCUMENT NUMBER: 131:23495
TITLE: Ion exchange chromatography for preparation of . **alpha.-lactalbumin**
INVENTOR(S): Svanborg, Catharina; Svensson, Malin Wilhelmina; Hakansson, Per Anders
PATENT ASSIGNEE(S): Swed.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926979	A1	19990603	WO 1998-IB1919	19981123
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9912541	A1	19990615	AU 1999-12541	19981123
EP 1032596	A1	20000906	EP 1998-955823	19981123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001524491	T2	20011204	JP 2000-522135	19981123

PRIORITY APPLN. INFO.:
GB 1997-24725 A 19971121
GB 1998-12202 A 19980605
WO 1998-IB1919 W 19981123

ED Entered STN: 10 Jun 1999

AB An ion exchange method for preparation of an oligomeric form of α-lactalbumin comprises exposing a source of α-lactalbumin, in which the α-lactalbumin is preferably in the globule-like state, to an ion exchange medium which has been pretreated with casein or an active component thereof, such as oleic acid, and recovering α-lactalbumin in an oligomeric form therefrom. Pretreatment of the ion exchange medium, particularly with casein derived from human milk, has been found to significantly improve yields of the oligomeric form of α-lactalbumin

and mean that it can readily isolated from readily available sources such as bovine α-lactalbumin. This form of α-lactalbumin is useful therapeutically, in particular as an antibacterial agent and also as an anticancer therapeutic. The occurrence of DNA fragmentation, indicative of apoptosis, was observed when tumor cells were treated with multimeric α-lactalbumin prepared by using a DEAE-trisacryl M ion exchange column.

IC ICM C07K014-76
ICS A61K038-38; B01D015-08

CC **63-3** (Pharmaceuticals)
Section cross-reference(s): **1**

IT Liquid chromatographic stationary phases
Liquid chromatographic stationary phases
(anion exchange; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Chelating agents
(calcium; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Fatty acids, uses
Lipids, uses
RL: MOA (Modifier or additive use); USES (Uses)
(casein; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Milk
Milk
(frozen; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Antibacterial agents
Antitumor agents
Ion exchange
Ion exchange liquid chromatography
Milk
(ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Caseins, uses
RL: MOA (Modifier or additive use); USES (Uses)
(ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Frozen foods
Frozen foods
(milk; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT Anion exchange liquid chromatography
Anion exchange liquid chromatography
(stationary phases; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

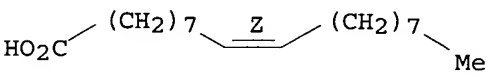
IT **Lactalbumins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(α -; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT 1185-53-1, TRIS hydrochloride
RL: PRP (Properties)
(buffer containing; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT 80701-61-7, DEAE-trisacryl M
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(column; ion exchange chromatog. for preparation of α -**lactalbumin** for therapeutic uses)

IT 60-00-4, EDTA, uses **112-80-1**, 9-Octadecenoic acid (9Z)-, uses
7647-01-0, Hydrochloric acid, uses 7647-14-5, Sodium chloride, uses
RL: MOA (Modifier or additive use); USES (Uses)
(ion exchange chromatog. for preparation of α - **lactalbumin** for therapeutic uses)
IT **112-80-1**, 9-Octadecenoic acid (9Z)-, uses
RL: MOA (Modifier or additive use); USES (Uses)
(ion exchange chromatog. for preparation of α - **lactalbumin** for therapeutic uses)
RN 112-80-1 HCAPLUS
CN 9-Octadecenoic acid (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

THE ESTIMATED COST FOR THIS REQUEST IS 63.60 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L40 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:117818 HCAPLUS
DOCUMENT NUMBER: 142:311612
TITLE: Stability of HAMLET - a kinetically trapped . **alpha.-lactalbumin** oleic acid complex
AUTHOR(S): Fast, Jonas; Mossberg, Ann-Kristin; Svanborg, Catharina; Linse, Sara
CORPORATE SOURCE: Department of Biophysical Chemistry, Lund University, Lund, SE-221 00, Swed.
SOURCE: Protein Science (2005), 14(2), 329-340
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The stability toward thermal and urea denaturation was measured for HAMLET (human α-lactalbumin made lethal to tumor cells) and α-lactalbumin, using CD and fluorescence spectroscopy as well as differential scanning calorimetry. Under all conditions examined, HAMLET appears to have the same or lower stability than α-lactalbumin. The largest difference is seen for thermal denaturation of the calcium-free (apo) forms, where the temperature at the transition midpoint is 15°C lower for apo HAMLET than for apo α-lactalbumin. The difference becomes progressively smaller as the calcium concentration increases. Denaturation of HAMLET was found to be irreversible. Samples of HAMLET that have been renatured after denaturation have lost the specific biol. activity toward tumor cells. Three lines of evidence indicate that HAMLET is a kinetic trap: (1) it has lower stability than α-lactalbumin, although it is a complex of α-lactalbumin and oleic acid; (2) its denaturation is irreversible and HAMLET is lost after denaturation; (3) formation of HAMLET requires a specific conversion protocol.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:6700 HCAPLUS
DOCUMENT NUMBER: 142:297209
TITLE: Manipulating the dietary cation-anion difference via drenching to early-lactation dairy cows grazing pasture
AUTHOR(S): Roche, J. R.; Petch, S.; Kay, J. K.
CORPORATE SOURCE: Dexcel Ltd., Hamilton, N. Z.
SOURCE: Journal of Dairy Science (2005), 88(1), 264-276
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diets fed to grazing dairy cows can vary considerably in their dietary cation-anion difference (DCAD; [Na + K - Cl]) and are often well in excess of what is considered optimal. The effects of DCAD on health and production of pasture-based dairy cows in early lactation were examined Four groups of 8 Holstein-Friesian dairy cows each were offered a generous daily allowance of pasture (45±6 kg dry matter [DM]/cow) for 35 days and achieved mean daily pasture intakes of .apprx.17 kg DM/cow. The cows were drenched twice daily with varying combinations of mineral compds. to achieve DCAD from +23 to +88 mEq/100 g DM. Linear increases in blood pH and HCO3- concns. and blood base excess and curvilinear increases in urine pH with increasing DCAD indicated nonrespiratory effect of DCAD on metabolic acid-base balance. Blood plasma concns. of Mg, K, and Cl declined as DCAD increased, whereas Na concns. increased. Urinary excretion of Ca decreased linearly as DCAD increased, although the data suggest that the decline may be curvilinear. These results in conjunction with the increased concns. of ionized Ca suggest that intestinal absorption of Ca or bone resorption, or both, increased as DCAD declined. The DM intake, as measured with nondigestible markers, was not much affected by DCAD. The linear increase in the yield of linolenic acid, vaccenic acid, and cis-9,trans-11-conjugated linoleic acid in milk as DCAD increased was consistent with pos. effects of DCAD on feed DM intake. Increasing DCAD did not much affect milk yield or milk protein, but the concentration and yield of milk fat linearly increased with increasing DCAD. The increased milk fat yield was mainly due to increased de novo biosynthesis in the mammary epithelial cells, although an increase in the yield of preformed fatty acids also occurred. Milk production data suggested that DCAD for optimal production on pasture diets may be higher than the +20 mEq/100 g DM previously recommended for total mixed rations.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:620445 HCAPLUS
DOCUMENT NUMBER: 141:256779
TITLE: Electrochemical Quartz Crystal Nanobalance Study of the Adsorption/Displacement Phenomena of Proteins and Lipids on Pt
AUTHOR(S): Wilson, Craig D.; Roscoe, Sharon G.
CORPORATE SOURCE: Department of Chemistry, Acadia University, Wolfville, NS, B4P 2R6, Can.
SOURCE: Langmuir (2004), 20(18), 7547-7556
CODEN: LANGD5; ISSN: 0743-7463
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The electrochem. quartz crystal nanobalance (EQCN) was used to measure the adsorption behavior of a series of lipids (stearate, oleate, linoleate, and γ-linolenate) on a Pt surface from a phosphate buffer pH 7.0 solution at 295 K and to investigate their adsorption/displacement behavior with the proteins, β-lactoglobulin and α-lactalbumin, which are known to cause fouling during milk processing. The EQCN technique and the complementary technique of cyclic voltammetry measured simultaneously provided information on the efficiency of solubilization of the proteins by these lipids. Excellent agreement was obtained for the surface concentration of adsorbed lipid from the surface charge d. from cyclic voltammetry measurements and the change in mass from the EQCN frequency measurements. The Gibbs energy of adsorption showed the lipids to have a strong affinity for the platinum surface. Addition of protein to a preadsorbed lipid layer showed α-lactalbumin to be able to coadsorb with the lipids, while β-lactoglobulin was able to desorb some of the unsatd. lipids but appeared to coadsorb with the saturated lipid, stearate. Addition of lipid to a preadsorbed protein layer showed the unsatd. lipids to be able to displace some of the protein. A comparison of the desorption ability of the lipids showed stearate to be very inefficient at removing protein, while the other three lipids were able to remove each of the proteins, with the order of efficiency for protein desorption being oleate > linoleate > γ-linolenate.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:573835 HCAPLUS
DOCUMENT NUMBER: 141:259531
TITLE: FT-Raman Spectroscopy, Fluorescent Probe, and Solvent Accessibility Study of Egg and Milk Proteins
AUTHOR(S): Alizadeh-Pasdar, Nooshin; Li-Chan, Eunice C. Y.; Nakai, Shuryo
CORPORATE SOURCE: Faculty of Agricultural Sciences, Food, Nutrition, and Health program, University of British Columbia, Vancouver, BC, V6T 1Z4, Can.
SOURCE: Journal of Agricultural and Food Chemistry (2004), 52(16), 5277-5283
CODEN: JAFCAU; ISSN: 0021-8561
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Due to possible contribution of both electrostatic and hydrophobic interactions, use of anionic fluorescent probes such as 1-anilinonaphthalene-8-sulfonic acid (ANS) and cis-parinaric acid (CPA) for the measurement of protein surface hydrophobicity (S0) has been controversial. A neutral probe, 6-propionyl-2-(dimethylamino)-naphthalene (PRODAN), may circumvent this problem. To select the best indicator of S0, the data for 9 model proteins in phosphate buffer, pH 7.5, measured using the above-mentioned probes, was compared to their FT-Raman spectra and calculated solvent accessibility values. Log S0 measured using CPA had the highest correlation (r = 0.874) with the intensities of Raman spectral signals at 760 cm-1 and 2800-3100 cm-1, which were combined using a mixture design based on the random-centroid optimization. The order of correlation of Raman spectral parameters with S0 values were CPA > PRODAN > ANS. FT-Raman spectroscopy, therefore, identified CPA, followed by PRODAN, as the fluorescent probe of choice for describing surface hydrophobicity. However, the amino acid surface accessibility calculated using the PredictProtein software was not useful in identifying the best

fluorescent probe for the measurement of S0.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:449884 HCAPLUS
DOCUMENT NUMBER: 140:420388
TITLE: Binary prediction tree modeling with many predictors and its uses in clinical and genomic applications
INVENTOR(S): Nevins, Joseph R.; West, Mike; Huang, Andrew T.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 886 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004038376	A2	20040506	WO 2003-XB33946	20031024
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004038376	A2	20040506	WO 2003-US33946	20031024
WO 2004038376	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:		
US 2002-420729P	P	20021024
US 2002-421062P	P	20021025
US 2002-421102P	P	20021025
US 2002-424701P	P	20021108
US 2002-424715P	P	20021108
US 2002-424718P	P	20021108
US 2002-425256P	P	20021112
US 2003-448461P	P	20030221
US 2003-448462P	P	20030221
US 2003-457877P	P	20030327
US 2003-458373P	P	20030331
WO 2003-US33946	A	20031024

AB The statistical anal. described and claimed is a predictive statistical tree model that overcomes several problems observed in prior statistical models and regression analyses, while ensuring greater accuracy and predictive capabilities. Although the claimed use of the predictive

statistical tree model described herein is directed to the prediction of a disease in individuals, the claimed model can be used for a variety of applications including the prediction of disease states, susceptibility of disease states or any other biol. state of interest, as well as other applicable non-biol. states of interest. This model first screens genes to reduce noise, applies kmeans correlation-based clustering targeting a large number of clusters, and then uses singular value decompns. (SVD) to extract the single dominant factor (principal component) from each cluster. This generates a statistically significant number of cluster-derived singular factors, that are referred to as metagenes, that characterize multiple patterns of expression of the genes across samples. The strategy aims to extract multiple such patterns while reducing dimension and smoothing out gene-specific noise through the aggregation within clusters. Formal predictive anal. then uses these metagenes in a Bayesian classification tree anal. This generates multiple recursive partitions of the sample into subgroups (the 'leaves' of the classification tree), and assocs. Bayesian predictive probabilities of outcomes with each subgroup. Overall predictions for an individual sample are then generated by averaging predictions, with appropriate wts., across many such tree models. The model includes the use of iterative out-of-sample, cross-validation predictions leaving each sample out of the data set one at a time, refitting the model from the remaining samples and using it to predict the hold-out case. This rigorously tests the predictive value of a model and mirrors the real-world prognostic context where prediction of new cases as they arise is the major goal.

L40 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:356702 HCAPLUS
DOCUMENT NUMBER: 141:84290
TITLE: Conformational analysis of HAMLET, the folding variant of human α -**lactalbumin** associated with apoptosis
AUTHOR(S): Casbarra, Annarita; Birolo, Leila; Infusini, Giuseppe; Dal Piaz, Fabrizio; Svensson, Malin; Pucci, Piero; Svanborg, Catharina; Marino, Gennaro
CORPORATE SOURCE: Dipartimento di Chimica Organica e Biochimica, Universita di Napoli Federico II, Naples, I-80126, Italy
SOURCE: Protein Science (2004), 13(5), 1322-1330
CODEN: PRCIEI; ISSN: 0961-8368
PUBLISHER: Cold Spring Harbor Laboratory Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A combination of hydrogen/deuterium (H/D) exchange and limited proteolysis expts. coupled to mass spectrometry anal. was used to depict the conformation in solution of HAMLET, the folding variant of human α-lactalbumin, complexed to oleic acid, that induces apoptosis in tumor and immature cells. Although near- and far-UV CD and fluorescence spectroscopy were not able to discriminate between HAMLET and apo-α-lactalbumin, H/D exchange expts. clearly showed that they correspond to two distinct conformational states, with HAMLET incorporating a greater number of deuterium atoms than the apo and holo forms. Complementary proteolysis expts. revealed that HAMLET and apo are both accessible to proteases in the β-domain but showed substantial differences in accessibility to proteases at specific sites. The overall results indicated that the conformational changes associated with the release of Ca2+ are not sufficient to induce the HAMLET conformation. Metal depletion might represent the first event to produce a partial unfolding in the β-domain of α-lactalbumin, but some more unfolding is needed to generate the active conformation HAMLET, very likely allowing

the protein to bind the C18:1 fatty acid moiety. On the basis of these data, a putative binding site of the oleic acid, which stabilizes the HAMLET conformation, is proposed.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:191049 HCAPLUS
DOCUMENT NUMBER: 141:6080
TITLE: A comparison of the composition, coagulation characteristics and cheesemaking capacity of milk from Friesian and Jersey dairy cows
AUTHOR(S): Auldist, Martin J.; Johnston, Keith A.; White, Nicola J.; Fitzsimons, W. Paul; Boland, Michael J.
CORPORATE SOURCE: Dexcel Ltd., Hamilton, 3123, N. Z.
SOURCE: Journal of Dairy Research (2004), 71(1), 51-57
CODEN: JDRSAN; ISSN: 0022-0299
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Twenty-nine multiparous cows of each of the Jersey and Friesian breeds, all κ-casein AB phenotype, were grazed together and managed identically. On 3 occasions during 10 d in spring (early lactation), milk was collected from all cows at 4 consecutive milkings and bulked according to breed. On a sep. occasion, milk samples were also collected from each cow at consecutive a.m. and p.m. milkings to form one daily sample per cow. The bulked milks (800-1000 L per breed on each occasion) were standardized to a protein:fat (P:F) ratio of 0·80, and 350 L from each breed was made into Cheddar cheese. The solids content of the remaining Friesian milk was then increased by ultrafiltration to a solids concentration equal to that of the Jersey milk. This solids-standardized Friesian milk and a replicate batch of P:F standardized Jersey milk were made into two further batches of Cheddar cheese in 350-l vats. Compared with Friesian milk, Jersey milk had higher concns. of most milk components measured, including protein, casein, and fat. There were few difference in milk protein composition between breeds, but there were differences in fat composition Friesian milk fat had more conjugated linoleic acid (CLA) than Jersey milk fat. Jersey milk coagulated faster and formed firmer curd than Friesian milk. Concns. of some milk components were correlated with coagulation parameters, but relationships did not allow prediction of cheesemaking potential. Jersey milk yielded 10% more cheese per kg than Friesian milk using P:F standardized milk, but for milks with the same solids concentration there were no differences in cheese yield. No differences in cheese composition between breeds were detected. Differences in cheesemaking properties of milk from Jerseys and Friesians were entirely related to the concns. of solids in the original milk.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:165494 HCAPLUS
DOCUMENT NUMBER: 140:405665
TITLE: Milk beyond food
AUTHOR(S): Sharma, R. S.
CORPORATE SOURCE: SMC College of Dairy Science, Anand, 388 110, India
SOURCE: Indian Journal of Agriculture, Environment & Bio-Technology (2003), 1(1), 1-22
CODEN: IJAECV
PUBLISHER: Indian Society of Agricultural Chemists
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Infancy is the only period of the life when one food is expected to provide the whole nutrition as well as to ensure protection against infection. For the mammalian species, the nature has devised an individual fluid food the milk which fulfill the requirement of energy and nutrients till the individual grows gradually and learns to be independent of such maternal support partially and completely. The milk of individual mammalian species is so designed that the major vital constituents like fat, protein, carbohydrates, vitamins and minerals are varied in level from species to species as per the requirement of their offspring. Man is the only species to use the milk of other mammals as food for adults and, in a modified form for its own infants. This is because milk is exclusive source of nutrients for young and a high grade source of dietary nitrogen and essential amino acids for adults. Being recognized as the most wholesome and complete single food available in nature, the World Health Organization has also earmarked consumption of 220 g of milk per day per person. Besides the primary role of milk to provide enough nutrients, the recent advances in food and nutrition sciences now support the concept the diet may have significant role to play in modulation of various function in body.

REFERENCE COUNT: 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:822567 HCAPLUS

DOCUMENT NUMBER: 139:392659

TITLE: HAMLET Interacts with Histones and Chromatin in Tumor Cell Nuclei

AUTHOR(S): Dueringer, Caroline; Hamiche, Ali; Gustafsson, Lotta; Kimura, Hiroshi; Svanborg, Catharina

CORPORATE SOURCE: Institute of Laboratory Medicine, Lund University, Lund, 223 62, Swed.

SOURCE: Journal of Biological Chemistry (2003), 278(43), 42131-42135
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB HAMLET is a folding variant of human α-lactalbumin in an active complex with oleic acid. HAMLET selectively enters tumor cells, accumulates in their nuclei and induces apoptosis-like cell death. This study examined the interactions of HAMLET with nuclear constituents and identified histones as targets. HAMLET was found to bind histone H3 strongly and to lesser extent histones H4 and H2B. The specificity of these interactions was confirmed using BIAcore technol. and chromatin assembly assays. In vivo in tumor cells, HAMLET co-localized with histones and perturbed the chromatin structure; HAMLET was found associated with chromatin in an insol. nuclear fraction resistant to salt extraction In vitro, HAMLET bound strongly to histones and impaired their deposition on DNA. We conclude that HAMLET interacts with histones and chromatin in tumor cell nuclei and propose that this interaction locks the cells into the death pathway by irreversibly disrupting chromatin organization.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:779797 HCAPLUS

DOCUMENT NUMBER: 140:58676

TITLE: Comparison of milk produced by cows cloned by nuclear

transfer with milk from non-cloned cows
AUTHOR(S): Walsh, Marie K.; Lucey, John A.; Govindasamy-Lucey, Selvarani; Pace, Marvin M.; Bishop, Michael D.
CORPORATE SOURCE: Nutrition and Food Sciences Department, Utah State University, Logan, UT, 84322, USA
SOURCE: Cloning and Stem Cells (2003), 5(3), 213-219
CODEN: CSCLBO; ISSN: 1536-2302
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors evaluated the composition of milk from 15 lactating non-embryonic cell cloned cows and six non-cloned lactating cows over a single season. The cloned cows came from five unique genetic lines and three distinct breeds. Milk samples were analyzed for total solids, fat, fatty acid profile, lactose, protein and compared to non-cloned and literature values. Gross chemical composition of milk from cloned cows was similar to that of the non-cloned cows and literature values. Our results lead us to conclude that there are no obvious differences in milk composition produced from cloned cows compared to non-cloned cows.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:134737 HCAPLUS
DOCUMENT NUMBER: 138:303203
TITLE: Lactational effect of propionic acid and duodenal glucose in cows
AUTHOR(S): Rigout, S.; Hurtaud, C.; Lemosquet, S.; Bach, A.; Rulquin, H.
CORPORATE SOURCE: Unite Mixte de Recherches Production du Lait, Institut National de Recherche Agronomique, Saint-Gilles, 35590, Fr.
SOURCE: Journal of Dairy Science (2003), 86(1), 243-253
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Five Holstein dairy cows were used in 5+5 Latin square design to compare the effects of 2 amts. of duodenal glucose or ruminal propionic acid (C3) on milk yield and composition Grass silage-based diet was supplemented with a mixture of volatile fatty acids (control) or pure C3 (1.72 and 3.45 Mcal/d) infused directly into the rumen or with glucose (1.72 and 3.45 Mcal/day) infused into the duodenum. The treatments were isoenergetic and isonitrogenous and contained resp. 100 and 115% of energy and protein requirements according to INRA 1989. Only C3 treatments modified rumen fluid volatile fatty acid composition and linearly increased the C3 levels up to 25.5%. Both treatments substantially decreased milk fat yield and content and linearly increased milk and milk protein yields. Although no significant differences between glucose and C3 were seen in milk yield and composition, the mechanisms involved in the milk fat level decrease may be different. Whereas the C3 treatments decreased the milk fatty acid production in a homogeneous way, with the glucose treatments the short-chain and long-chain fatty acids production decreased and medium-chain fatty acids production increased. A bibliog. study confirmed that increasing dietary glucogenic precursors (GP) supply can curvilinearly increase milk yield, linearly increase milk protein content (0.04%/Mcal GP), and curvilinearly decrease milk fat content (0.14%/Mcal GP). Thus, it is important to account for the nature of dietary energy supplied by the ration formulation.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:849134 HCAPLUS
DOCUMENT NUMBER: 138:68634
TITLE: Molten globule of bovine α - **lactalbumin** at neutral pH induced by heat, trifluoroethanol, and oleic acid: a comparative analysis by circular dichroism spectroscopy and limited proteolysis
AUTHOR(S): De Laureto, Patrizia Polverino; Frare, Erica; Gottardo, Rossella; Fontana, Angelo
CORPORATE SOURCE: CRIBI Biotechnology Centre, University of Padua, Padua, 35121, Italy
SOURCE: Proteins: Structure, Function, and Genetics (2002), 49(3), 385-397
CODEN: PSFGEY; ISSN: 0887-3585
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The calcium-depleted form of α-lactalbumin (α-LA) at neutral pH can be induced to adopt a partly folded state or molten globule upon moderate heating, by dissolving the protein in aqueous TFE or by adding oleic acid. This last folding variant of the protein, named HAMLET, can induce apoptosis in tumor cells. The aim of the present work was to unravel from CD (CD) measurements and proteolysis expts. structural features of the molten globule of apo-α-LA at neutral pH. CD spectra revealed that the molten globule of apo-α-LA can be obtained upon mild heating at 45°, as well as at room temperature in the presence of 15% TFE or by adding to the protein solution 7.5 equiv of oleic acid. Under these various conditions the far- and near-UV CD spectra of apo-α-LA are essentially identical to those of the most studied molten globule of α-LA at pH 2.0 (A-state). Proteolysis of the 123-residue chain of apo-α-LA by proteinase K at 4° occurs slowly as an all-or-none process leading to small peptides only. At 37°, proteinase K preferentially cleaves apo-α-LA at peptide bonds Ser34-Gly35, Gln39-Ala40, Gln43-Asn44, Phe53-Gln54, and Asn56-Asn57. All these peptide bonds are located at level of the β-subdomain of the protein (chain region 34-57). Similar sites of preferential cleavage have been observed with the TFE- and oleic acid-induced molten globule of apo-α-LA. A protein species given by the N-terminal fragment 1-34 linked via the four disulfide bridges to the C-terminal fragment 54-123 or 57-123 can be isolated from the proteolytic mixture The results of this study indicate that the same molten globule state of apo-α-LA can be obtained at neutral pH under mildly denaturing conditions, as indicated by using a classical spectroscopic technique such as CD and a simple biochem. approach as limited proteolysis. We conclude that the molten globule of α-LA maintains a native-like tertiary fold characterized by a rather well-structured α-domain and a disordered chain region encompassing the β-subdomain 34-57 of the protein.
REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:129194 HCAPLUS
DOCUMENT NUMBER: 132:276538
TITLE: A folding variant of α - **lactalbumin** with bactericidal activity against Streptococcus pneumoniae

AUTHOR(S): Hakansson, Anders; Svensson, Malin; Mossberg, Ann-Kristin; Sabharwal, Hemant; Linse, Sara; Lazou, Irene; Lonnerdal, Bo; Svanborg, Catharina
CORPORATE SOURCE: Department of Microbiology, Immunology and Glycobiology, Institute of Laboratory Medicine, Lund University, Lund, SE-223 62, Swed.
SOURCE: Molecular Microbiology (2000), 35(3), 589-600
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study describes an α-lactalbumin folding variant from human milk with bactericidal activity against antibiotic-resistant and -susceptible strains of Streptococcus pneumoniae. The active complex precipitated with the casein fraction at pH 4.6 and was purified from casein by a combination of anion exchange and gel chromatog. Unlike other casein components, the active complex was retained on the ion-exchange matrix and eluted only with high salt. The eluted fraction showed N-terminal and mass spectrometric identity with human milk α-lactalbumin, but native α-lactalbumin had no bactericidal effect. Spectroscopic anal. demonstrated that the active form of the mol. was in a different folding state, with secondary structure identical to α-lactalbumin from human milk whey, but fluctuating tertiary structure. Native α-lactalbumin could be converted to the active bactericidal form by ion-exchange chromatog. in the presence of a **cofactor** from human milk casein, characterized as a C18:1 **fatty acid.** Anal. of the antibacterial spectrum showed selectivity for streptococci; Gram-neg. and other Gram-pos. bacteria were resistant. The folding variant of α-lactalbumin is a new example of naturally occurring mols. with antimicrobial activity.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:799270 HCAPLUS
DOCUMENT NUMBER: 132:107135
TITLE: Associations among individual proteins and fatty acids in bovine milk as determined by correlations and factor analyses
AUTHOR(S): Bobe, Gerd; Beitz, Donald C.; Freeman, Albert E.; Lindberg, Gary L.
CORPORATE SOURCE: Nutritional Physiology and Animal Breeding Groups, Department of Animal Science, Iowa State University, Ames, IA, 50011-3150, USA
SOURCE: Journal of Dairy Research (1999), 66(4), 523-536
CODEN: JDRSAN; ISSN: 0022-0299
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Assocns. among quantities and concns. of individual milk proteins and fatty acids were determined in individual milk samples from 233 Holstein cows. Correlation coeffs. among the six major proteins and the eleven major fatty acids in bovine milk were grouped hierarchically. Factor analyses grouped the milk components into seven families: fatty acids 4:0-6:0, 6:0-16:0, 16:0, 18:0, 16:1 plus 18:1 plus 18:2, all milk proteins and β-lactoglobulin alone. Correlation coeffs. and groupings by factor analyses coincided with shared pathways of synthesis or genetic origins of milk proteins and fatty acids because they are the basis of the correlation coeffs. Hence, the results from correlations and factor

analyses could be used to develop hypotheses for the synthesis of milk components and other coordinately regulated physiol. processes.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:94782 HCAPLUS
DOCUMENT NUMBER: 130:251674
TITLE: Nutritional influences on the composition of milk from cows of different protein phenotypes in New Zealand
AUTHOR(S): Mackle, T. R.; Bryant, A. M.; Petch, S. F.; Hill, J. P.; Auldist, M. J.
CORPORATE SOURCE: Dairying Research Corporation Ltd., Hamilton, N. Z.
SOURCE: Journal of Dairy Science (1999), 82(1), 172-180
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of contrasting nutritional regimens on milk composition from cows of different protein phenotypes were studied in 20 sets of seasonally calving identical twin cows that constituted 5 different protein phenotypes (4 sets of twins per phenotype). The cows were subjected to 2 nutritional treatments in crossover expts. during spring (early lactation) and summer (mid to late lactation). The nutritional treatments were ad libitum grazing (.apprx.40 kg dry matter/day per cow) plus 5 kg of barley-based concentrate and restricted grazing (.apprx.20 kg dry matter/day per
cow). The phenotypes studied allowed comparisons of the AA, AB, and BB variants of both β-lactoglobulin (β-LG) and κ-casein.
Milk samples were collected from each cow near the end of each 14-day treatment period and were analyzed for individual protein and fat constituents. The diets had significant effects on the concns. of all milk components measured. The protein phenotypes affected some protein components but not fat components. Interactions between the effects of β-LG phenotype and diet were noted for the concns. of some milk components. Diet and protein phenotype have important effects on the manufacturing potential of milk produced under the dairying systems of New Zealand which rely heavily on grazing. The effects of nutrition on milk composition may depend on the β-LG phenotype.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:167804 HCAPLUS
DOCUMENT NUMBER: 128:269993
TITLE: Forage of different physical forms in the diets of lactating Granadina goats: Nutrient digestibility and milk production and composition
AUTHOR(S): Sampelayo, M. R. Sanz; Perez, L.; Boza, J.; Amigo, L.
CORPORATE SOURCE: Estacion Experimental del Zaidin, Consejo Superior de Investigaciones Cientificas, Departamento de Nutricion Animal, Granada, 18008, Spain
SOURCE: Journal of Dairy Science (1998), 81(2), 492-498
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of energy balance and diet phys. characteristics on milk production were studied in feeding and digestion trials with 10 Granadina goats in 2 groups. The concentrate fraction of both diets was the same, but the

forage fraction was in the form of long alfalfa hay or pelleted alfalfa. The feed intake and forage/concentrate ratio of the two diets were not different, although the diet with pellets was more digestible. The milk fat and protein levels depended on dietary energy intake, but not on the dietary treatment. The milk protein in goats fed the pelleted diet was higher in casein. No sensible differences were noted in the fatty acid composition of the milk. Nitrogen and metabolizable energy utilization for milk production was greater in goats fed the pelleted diet. It may be advantageous to use pelleted alfalfa rather than alfalfa hay in the dairy goat diets.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:790698 HCAPLUS
DOCUMENT NUMBER: 128:125056
TITLE: Interactions of α -**lactalbumin** with fatty acids and spin label analogs
AUTHOR(S): Cawthern, Kevin M.; Narayan, Mahesh; Chaudhuri, Dipankar; Permyakov, Eugene A.; Berliner, Lawrence J.
CORPORATE SOURCE: Departments of Chemistry and Medical Biochemistry and the Biophysics Program, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Biological Chemistry (1997), 272(49), 30812-30816
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bovine α-lactalbumin (I) was shown by intrinsic protein fluorescence and ESR methods to interact with the spin-labeled fatty acid analog, 5-doxylstearic acid, as well as stearic acid. An intrinsic fluorescence titration of various I forms with 5-doxylstearic acid caused 1st an increase and then a decrease in emission intensity with concomitant shifts in Trp emission wavelength. In some cases, up to 3 steps in the fluorescence titration curves were visible, which were fit to apparent binding steps from 10-6 to 10-4 M. The binding parameters of 5-doxylstearic acid for apo-I and Ca2+-I were an order of magnitude different from one another; the stronger one, apo-I, exhibited a Kd of 35 μM. ESR titrns. of 5-doxylstearic acid-loaded apo-I with stearate (micelles) appeared to suggest sep. binding loci if I indeed binds stearate at these concns. The titration of I by stearic acid resulted in a fluorescence emission red shift and an apparent stepped increase in fluorescence intensity. Lipid-protein association occurred at concns. at which stearic acid micelles and aggregates began to form in the absence of protein. Nonetheless, the relatively strong association between stearic acid and apo-I was also confirmed by means of the fluorescent indicator, acrylodated fatty acid binding protein, in which the addition of I to the stearate-loaded indicator protein reversed the decrease in fluorescence of the acrylodan chromophore conjugated to the protein.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:30982 HCAPLUS
DOCUMENT NUMBER: 126:72929
TITLE: Chemical composition of bovine colostrum
AUTHOR(S): Guo, Benheng; Luo, Chengxiang
CORPORATE SOURCE: Northeast Agricultural University, Harbin, 150030,

Peop. Rep. China
SOURCE: Journal of Northeast Agricultural University (English Edition) (1996), 3(1), 72-77
CODEN: JNAUFJ; ISSN: 1006-8104
PUBLISHER: Northeast Agricultural University
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chemical compns. of bovine colostrum and their change after parturition were studied. Fat, total protein, whey proteins, ash and total solid were higher than those in milk and decreased as lactation time was increased. Lactose was lower than that in milk and increased with the increase of lactation time. Whey proteins of colostrum such as Ig, β-Lg, BSA, Lf and Lp were obviously higher than those in milk and decreased as lactation time was increased. There were high unsatd. fatty acids in colostrum compared with bovine milk. Na, Cl, Fe, Zn, Cr and Mg in colostrum were higher than those in milk. They fell as lactation time was increased. I, K, P, Mn and Cu increased with the increase of lactation time. Co, As and Pb were not detected by ICP method.

L40 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:595037 HCAPLUS
DOCUMENT NUMBER: 123:81954
TITLE: Chemical and physical characteristics of mare's milk
AUTHOR(S): Pagliarini, E.; Solaroli, G.; Peri, C.
CORPORATE SOURCE: Sezione Tecnologie Alimentari, Universita degli Studi di Milano, Milan, 20133, Italy
SOURCE: Italian Journal of Food Science (1995), (Spec. Issue), 40-9
CODEN: ITFSEY; ISSN: 1120-1770
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Data on the chemical composition and phys. properties of mare's milk are presented. A comparison between these data and those obtained for cow's milk shows that the levels of fat and cholesterol of mare's milk are about one third those of cow's milk. The ratio between unsatd. and saturated fatty acids is 1.32 (0.45 for cow's milk), and the ratio between polyunsatd. and monounsatd. fatty acids is 0.83 (0.08 for cow's milk). Fifty percent of the protein fraction consists of whey proteins, and the lysozyme content (11%) is very high. Mare's milk has a very high vitamin C content and a low mineral content. The Ca/P ratio is 1.7, which is very close to the optimal value for calcium assimilability.

L40 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:313212 HCAPLUS
DOCUMENT NUMBER: 122:159057
TITLE: The development of squid (Todarodes pacificus) sik-hae in Kang-Nung district. 2. The effects of fermentation temperatures and periods on chemical and microbial changes, and the partial purification of protease
AUTHOR(S): Kim, Sang-Moo; Cho, Young-Je; Lee, Keun-Tai
CORPORATE SOURCE: Department of Fisheries Resources Development, Kangnung National Univ., Kangnung, 210-702, S. Korea
SOURCE: Han'guk Susan Hakhoechi (1994), 27(3), 223-31
CODEN: HSHKAW; ISSN: 0374-8111
PUBLISHER: Korean Fisheries Society
DOCUMENT TYPE: Journal
LANGUAGE: Korean
AB In order to develop the squid(Todarodes pacificus) sik-hae, the changes of TBA, fatty acids, free amino acids, and the number of microflora fermented at different fermentation temps. and periods were determined In addition, protease

from squid sik-hae was partially purified. The number of TBA was the highest after 5-day storage and decreased after that, and lipid oxidation was the highest at 10°C. The amts. of linoleic acid(18:2) and oleic acid (18:1) were about 60% of fatty acid composition of squid sik-hae, and linolenic acid(18:3) and EPA(20:5) significantly decomposed with increasing fermentation periods and temps. Pro, His, Arg, leu, and Glu were composed mainly of amino acid and the composition ratios of Ser, His, and Arg decreased with increasing fermentation periods whereas, those of Glu, Ala, Val, and Tyr increased. The composition ratios of Glu, Val, and Met increased with increasing fermentation temps. whereas, those of Ala, Cys, Thr, and Gly decreased. The number of microflora generally increased up to 15-days of storage and decreased after that. The rates of increase and decrease of the microbial number increased in proportion to fermentation temps. In addition, the bacteria producing proteases were identified as Bacillus spp. Proteases from 60 .apprx. 80% ammonium sulfate concentration showed the highest activity and had about 15 binds with mol. wts. between 20,000 and 40,000 Dalton by SDS-PAGE.

L40 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:42557 HCAPLUS
DOCUMENT NUMBER: 122:8435
TITLE: Isolation of lipase-active fractions from ultra-high temperature-processed milk and their patterns of releasing fatty acids from milk fat emulsion
AUTHOR(S): Choi, I. W.; Jeon, I. J.; Smith, J. S.
CORPORATE SOURCE: Department of Animal Sciences and Industry, Kansas State University, Manhattan, KS, 66506-1600, USA
SOURCE: Journal of Dairy Science (1994), 77(8), 2168-76
CODEN: JDSCAE; ISSN: 0022-0302
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To examine residual lipase activities in UHT-processed milk samples, two protein isolates were prepared, one from aqueous supernatant and the other from milk fat globule membrane. Results of DEAE-cellulose chromatog. indicated that the protein isolates from the aqueous supernatants contained three lipase-active fractions; the proteins from the milk fat globule membranes exhibited only one lipase-active fraction. Anal. by SDS-PAGE revealed that the lipase-active fractions from the aqueous supernatants contained a major or minor κ-casein component, as well as other caseins and whey proteins. However, the lipase-active fraction from the milk fat globule membranes was composed mainly of α-casein. When a pool of aqueous supernatants was incubated with a milk fat emulsion at 35°C for 4 h, the fractions hydrolyzed butyric acid the most, followed by caproic and palmitic acids. However, the lipase-active fraction from the milk fat globule membranes hydrolyzed palmitic and stearic acids most, followed by linoleic and oleic acids.

L40 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:71046 HCAPLUS
DOCUMENT NUMBER: 120:71046
TITLE: The reactions of ozone with proteins and unsaturated fatty acids in reverse micelles
AUTHOR(S): Uppu, Rao M.; Pryor, William A.
CORPORATE SOURCE: Biodyn. Inst., Louisiana State Univ., Baton Rouge, LA, 70803-1800, USA
SOURCE: Chemical Research in Toxicology (1994), 7(1), 47-55
CODEN: CRTOEC; ISSN: 0893-228X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Sodium oleate cosolubilized with lysozyme in reverse micellar solns. is shown to inhibit the ozone-mediated oxidation of tryptophan residues in the protein. The magnitude of inhibition by oleate, which is an direct measure of the fraction of ozone that reacts with oleate instead of the protein, is predictable using a kinetic model that is based on the concns. and the reactivities toward ozone of the amino acid residues in lysozyme and the double bond in oleate. Oleate (2 mM), linoleate (1 mM), linolenate (0.67 mM), and γ-linolenate (0.67 mM) all inhibit the ozonation of lysozyme similarly; this indicates that ozone reacts with double bonds in mono-, di-, or polyunsatd. fatty acids at approx. the same rate. All these fatty acids reside at the micellar interface with their lead groups facing inward toward the dispersed water pools and the hydrocarbon tails projecting into the bulk, continuous organic phase. Various short-chain 2-, 3-, and 4-alkenoic acids that reside predominantly in the water pools, and long-chain alkenes that reside in the bulk organic solvent, have a similar inhibitory effect on the ozone-mediated oxidation of tryptophan residues in lysozyme. Thus, the location of olefinic compds. in the micelles or bulk organic phase per se does not influence the rate of reaction in this reverse micellar system. A number of proteins that reside in the water pools of reverse micelles are found to behave similarly to lysozyme, including albumin, carbonic anhydrase, β-casein, α-chymotrypsin, α-lactalbumin, β-lactoglobulin, papain, apotransferrin, trypsin, and trypsin inhibitor. For all these proteins, the kinetic model predicts the fraction of ozone that reacts with tryptophan residues in the proteins and the protection offered by olefinic compds. The significance of these findings is discussed in relation to the reaction of ozone with proteins and unsatd. lipids in vivo in milieu where both occur, such as the lung lining fluid layer and biol. membranes.

L40 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:80291 HCAPLUS
DOCUMENT NUMBER: 114:80291
TITLE: Foaming oil-in-water compositions containing fats and oils, lactalbumins, glycerides, stabilizers, and sauce compositions for whipped condiments
INVENTOR(S): Ihara, Kiyoshi; Miyamoto, Makoto; Tsujinaka, Takuya; Kitamura, Akihiro; Nishiama, Toshihiko
PATENT ASSIGNEE(S): Kanegafuchi Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02215367	A2	19900828	JP 1989-35650	19890215
JP 07083692	B4	19950913		

PRIORITY APPLN. INFO.: JP 1989-35650 19890215

AB The title compns. comprise (A) oil-in-water compns. containing fats and oils 8-52, (enzyme-treated) lactalbumins 0.1-5, ≥1 emulsifiers chosen from polyglycerin fatty acid esters and organic acid monoglycerides 0.05-1, and ≥1 stabilizers chosen from α-starch, enzyme-treated gelatin, xanthan gum, pectin, and guar gum 0.01-1 weight% and (B) sauce compns. containing food materials, seasonings, spices, etc. A mixture of H2O 49.0 (based on total oil-in-water composition), lactalbumin 1.5, and hexaglycerin monostearate 0.4% was emulsified with a mixture of hydrogenated rapeseed oil 29, cotton seed oil 19.7, and citric acid monoglyceride 0.4% at 60°, mixed with 1.0% α-starch, sterilized, and homogenized

to manufacture an oil-in-water composition A sauce composition comprising brown mustard
80.2, lemon juice 16.5, and H2O 3.3% were whipped with the oil-in-water composition at 3 : 7 ratio, preserved at -20° for 3 mo, and chicken was decorated with the composition The composition was stable at 15° for ≥24 h and showed soft texture and good mouth melting.

L40 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:66707 HCAPLUS
DOCUMENT NUMBER: 104:66707
TITLE: Milk composition of rats feeding restricted litters
AUTHOR(S): Grigor, Murray R.; Allan, Janice; Carne, Alan; Carrington, Janet M.; Geursen, Arie
CORPORATE SOURCE: Dep. Biochem., Univ. Otago, Dunedin, N. Z.
SOURCE: Biochemical Journal (1986), 233(3), 917-19
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Milk samples were taken from rats feeding 10 pups and from both the suckled and nonsuckled glands of rats feeding 2 pups. The lipid, protein, and lactose concns. were similar in the milks from the secreting glands, but the fluid from the nonsuckled glands contained less lactose and lipid but significantly higher total protein and transferrin concns. The fatty acid compns. of the milk from the 3-sources were very similar. The mammary tissue from the rats feeding 10 pups had a higher DNA content per g wet weight than did either the suckled or nonsuckled mammary tissue of the rats feeding 2 pups. The specific activities of several lipogenic enzymes were significantly lower in the nonsuckled mammary tissue.

=>